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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/069,977	03/13/2002	Takakazu Inoue	020159	2998

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EXAMINER	
TUNG, JOYCE	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 07/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/069,977	INOUE, TAKAKAZU	
	Examiner	Art Unit	
	Joyce Tung	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/24/2003, 2/6, 4/29 and 5/21/2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-9 and 12-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-9 and 12-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

As requested on 4/29/2004 and 5/21/2004 and as set forth in the Petition filed 11/24/2003 under 1.81 to withdraw the finality of the Office action mailed 9/24/2003, the non-final Office action is issued as follows. According to the amendment filed 7/10/2004, which has been entered, claims 4-9 and 12-16 are pending.

1. The rejection of claims 1-14 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No.6, 287,769 is withdrawn.

2. The rejection of claims 1-9 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11-17 of U.S. Patent No.6274306 is withdrawn.

3. The objections of claims 4 and 14 are withdrawn.

4. The rejections of claims 10-14 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

5. The rejection of claims 1-2 and 9 under 35 U.S.C. 102(b) as being anticipated by Hamad et al. (Journal of Applied Microbiology, 1997, Vol. 83, 764-770) is withdrawn.

6. The rejection of claims 10-11 under 35 U.S.C. 102(b) as being anticipated by Wilding et al. (5,498,392) is withdrawn.

7. The rejection of claims 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hamad et al. (Journal of Applied Microbiology, 1997, Vol. 83, 764-770) as applied to claims 1-2 and 9 above, and further in view of Mullis et al. (4,800,159) is withdrawn.

8. Claims 4-5, 7-9 and 12-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hamad et al. (Journal of Applied Microbiology, 1997, Vol. 83, 764-770), in view of Wilding et al. (5,498,392).

Hamad et al. disclose a method of studying microflora of Sudanese sorghum flour (See pg. 764, the Abstract). Seven strains of *Lactobacillus* were isolated, representing the dominant flora (See pg. 764, the Abstract). The DNA was isolated from *lactobacilli* (See pg. 765 column 1, five paragraph). RAPD-PCR was performed with an arbitrary primer (See pg. 765, column 1, seventh paragraph). The primers used in the method of Hamad have specificity. The agarose electrophoresis patterns were visualized by ethidium bromide staining (See pg. 765, column 2, first paragraph). Hamad et al. also disclose that the partial sequences of the 16S rRNA of all three strains were found to be identical with that of *Lact. vaginalis* (See pg. 766, column 2, last paragraph). The 16S rRNA would have been amplified by using the same primer, which amplifies *Lact. vaginalis*. The teachings of Hamad et al. suggest that the primer used which has a sequence capable of amplifying a nucleic acid region coding 16S rRNA of said intestinal bacterium.

Hamad et al. do not disclose using a detector on which said probe are arranged on specific positions in a detector for analyzing an intestinal bacterial flora.

Wilding et al. disclose a device for PCR, which includes a detector. The detector has a probe located (See column 4, lines 52-55 and column 11, lines 56-61). Wilding et al. that disclose the PCR reaction cycle is complete and then the sample is to be detected (See column 15, lines 11-16). The detection region includes a labeled polynucleotide probe to detect the amplified polynucleotide (See column 4, lines 45-60).

One of ordinary skill in the art would have been motivated to apply the device of Wilding et al. to the method of Hamad et al. for analyzing the intestinal bacteria flora of a subject. The motivation is that the device of Wilding et al. is for conducting a polynucleotide polymerization

reaction to enable the rapid amplification of a polynucleotide in a sample and the device of Wilding et al. includes a detection region, which would have been convenient for performing the detection without contamination. It would have been prima facie obvious to carry out the method of analyzing an intestinal bacterial flora via amplifying the DNA from a subject and hybridizing the amplified DNA with a specific probe positioned on a detector.

The response filed 7/10/2004 argues that Hamad et al. do not teach any study on nucleic acid of an intestinal bacterial group in a sample extracted from a subject and Wilding also does not teach this. However, Hamad et al. disclose the study of bacterial flora of Sudanese sorghum flora and the sorghum flour contains the bacterial flora, for example, *Enterococcus faecalis,* (See pg. 764, the Abstract) which is an intestinal bacteria flora. Although Hamad et al. do not disclose the intestinal bacterial flora from a subject, one of ordinary skill would have been motivated to apply the method of Hamad et al. to analyzing the intestinal bacterial flora from a subject because of the teachings of Hamad et al. set forth above that Hamad et al. disclose that the partial sequences of the 16S rRNA of all three strains were found to be identical with that of *Lact. vaginalis* (See pg. 766, column 2, last paragraph). The 16S rRNA would have been amplified by using the same primer, which amplifies *Lact. vaginalis.* Thus, *the* teachings of Hamad et al. suggest the primer used which has a sequence capable of amplifying a nucleic acid region coding 16S rRNA of said intestinal bacteria flora. Wilding discloses a device for amplifying a preselected polynucleotide (See the Abstract).

The response filed 7/10/2004 further argues that Wilding et al. and Hamad et al. do not teach rapid simultaneous detection of a plurality of bacteria. However, the method of Hamad et al. was applied to detect a plurality of bacteria since the Sorghum flour contained more than one bacteria (See pg. 765, column 2, third paragraph and pg. 766, column 2, first paragraph and second paragraph). Wilding et al. disclose that the substrate may comprise a plurality of detection/ reaction chambers to enable the rapid parallel detection of polynucleotides in a

mixture (See column 5, lines 9-11). Based upon the teachings of Hamad et al. and Wilding et al. one of ordinary skill in the art would have been motivated to apply the device of Wilding et al. in the method of Hamad et al. for analyzing an intestinal bacterial flora of a subject.

Based upon the analysis above, the rejection is maintained.

9. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hamad et al. (Journal of Applied Microbiology, 1997, Vol. 83, 764-770) in view of Wilding et al. (5,498,392) as applied to claims 4-5, 7-9 and 12-16 above, and further in view of Mullis et al. (4,800,159).

The teachings of Hamad et al. and Wilding et al. are set forth in section 8 above.

Hamad et al. do not disclose probes to hybridize to said amplified fragment and that the amplified nucleic acid is used as a probe for detecting an intestinal bacterial flora.

Mullis et al. disclose a method of polymerase chain reaction for synthesizing the desired nucleic acid sequence and detecting the sequence amplified (See the Abstract). The amplification products were detected by labeled probe (See column 3, lines 16-17).

The teachings of Mullis et al. suggest that the intestinal bacterial flora would have been amplified and detected by hybridizing a nucleic acid probe. The amplified nucleic acid would have been used as probe because the amplified nucleic acid would have the same specificity as the probe used for the detection.

One of ordinary skill in the art at the time of the instant invention would have been motivated to apply the teachings of making the probe used in the method of Mullis et al. to analyze the intestinal bacterial flora of a subject because using probes to hybridize to an amplified nucleic acid products is specific for detection. It would have been prima facie obvious to apply the teachings of making probe to detect the amplified nucleic acid sequence of an intestinal bacterial flora in order to analyze the intestinal bacterial flora.

The response filed 7/10/2004 argues that the method of Mullis et al. only amplifies a desired single type of DNA fragment and the present invention requires that DNA fragment of a

plurality of bacteria are simultaneously amplified and detected by probes arranged on specific positions. Regarding the issue of the plurality of bacteria analyzed and the probes used for the analysis, it has been discussed in section 8 above (See section 8 above). The reference of Mullis et al. provided is for teaching of making the probe, which is from the amplified nucleic acid. Based upon the discussion in section 8 above and this section, the rejection is maintained.

New Grounds of Rejections Necessitated by the Amendments

Claim Rejections - 35 USC § 112

10 The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

11. Claims 12-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 12-16 are vague and indefinite because claims 12-13 depend from the canceled claim 11. In addition, the phrases "the apparatus", "said hybridizer" in claims 12-13, "said nucleic acid amplifier" in claim 14 have no antecedent basis.

b. Claims 12-16 are vague and indefinite because the language "in which is arranged a probe" is unclear whether the DNA chip has an immobilized probe arranged or not. Furthermore, regarding the language "having a nucleic acid sequence occurring", it is unclear whether the nucleic acid sequence is comprised by the genome of the intestinal bacterial. Clarification is required.

Summary

12. No claims are allowed.

13. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (703) 308-1119 on Monday-Friday from 10:00 AM-6:00 PM.

Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

14. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1637 via the PTO Fax Center located in Crystal Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung
June 7, 2004

GARY BENZION, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600
6/28/04